GLASS-IONOMER CEMENTS CONTAINING AMINO ACIDS

BACKGROUND OF THE INVENTION

Glass-ionomer cements were first developed about thirty years ago [1]. Glass-ionomer cements typically contain an ionic polymer composition such as an acrylic acid homo- or co-polymer, and a reactive glass composition such as a calcium fluoride- alumino-silicate glass powder. The ionic polymer is provided in aqueous liquid form, and the reactive glass is provided in powdery form. When these two compositions are mixed in water, a cement setting reaction takes place. These cements are known for their unique properties such as direct adhesion to tooth structure and base metal [2, 3], anticariogenic properties due to release of fluoride [4], thermal compatibility with tooth enamel and dentin because of low coefficients of thermal expansion similar to those of tooth structure [5], minimized microleakage at the tooth-enamel interface due to low shrinkage [6], biological compatibility and low cytotoxicity [7,8]. An acid-base interaction plays a major role in conventional glass-ionomer cements or self-cured cements [9, 10]. A similar interaction occurs when the cement contacts tooth enamel or dentin, which mainly contains hydroxyapatite (Ca^{2+} and PO^{4-}), and Type I collagen [6, 11]. Salt bridge formation is an essential aspect to the adhesion. Due to the salt bridges that form between the cement and tooth surfaces, these cements have been particularly useful as dental adhesives and anterior tooth restoratives [9].

Like enamel and dentin, bone also contains hydroxyapatite and Type I collagen [6, 11]. Based on the compositions, bone is very similar to dentin [6]. This is the basis for using glass-ionomer cements for bone adhesives and repair applications. Conventional bone cements are acrylate cements that provide fixation of a prosthesis through a so-called "mechanical interlock" between the acrylate resins and porous

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bone structures [12]. Unlike conventional bone cements, the glass-ionomer cements adhere to bone by means of formation of ionic bonding or salt-bridges. If hybrid systems (containing vinyl and carboxylic acid functionalities) are introduced, *in*
5   *situ* polymerization occurs through both groups and dual-curing cements form. As a result, the salt bridges and the mechanical interlocks together play an important role in strengthening the interfacial bonding [6, 11, 13].

Conventional glass-ionomer cements have been used as bone
10 cements [14-16]. Two glass-ionomer-type bone cements are manufactured in Germany, one called IONOS, and the other called Ionocerm. They are two-component systems, in which one component is composed of a copolymer of acrylic and maleic acid in aqueous solution and the second is a calcium-aluminum-
15 fluoro-silicate glass [14-15]. These formulations are similar to the dental glass-ionomer cements manufactured by ESPE Dental Co. (Germany)[17]. One preliminary study on otological surgery showed that these cements were very promising in terms of both adhesion and biocompatibility [14]. Another study
20 showed that they proved valuable in translabyrinthine acoustic neuroma surgery in that that the cements were easy to use, and did not cause observable side effects [15]. Negative results related to lower bonding strengths have been reported, however, [16]. Literature reporting further developments in
25 orthopaedic applications of glass-ionomer cements is sparse, however.

Commercial dental conventional glass-ionomer cement systems, such as poly(acrylic acid) or poly(acrylic acid-co-itaconic acid), have shortcomings. Problems associated with
30 brittleness and low tensile and flexural strengths have limited use of the current conventional glass-ionomer cements to certain low stress-bearing sites such as Class III and Class V cavities. Two major problems regarding the polymer

matrix are believed to exist. One problem resides in the direct or very close attachment or proximity of all the carboxylic acid (COOH) groups to the polymer backbone. Not all the carboxyl groups of polyacids are converted to

5   carboxylate groups during the course of the reaction and utilized in salt-bridge formations [18, 19]. Some free COOH groups remain unreacted because they are inaccessible due to steric hindrance. Also, when the polyacrylate chain is largely ionized, the remaining hydrogen becomes firmly bound

10 by electrostatic forces. As a result, the metal ions are increasingly hindered in their movement and capability to react at carboxyl sites. The speculation is that the strength and fracture resistance of the material are weakened due to this steric hindrance, which brings about significantly

15 reduced interactions between aluminum cations (Al++) and carboxylate anions (COO-) (and thus less cluster or salt bridge formation) in the cement.

The second problem deals with molecular weight. It is well-known that mechanical strengths are very much dependent

20 upon molecular weight, except for those primary chemical interactions [20]. Increase in molecular weight enhances the mechanical performance of the materials [21]. The molecular weight of highly ordered poly(acrylic acid) and its copolymers are severely limited by a polyelectrolyte effect. Introduction

25 of monomers with various spacer lengths for the carboxylic acid may serve to increase the molecular weight of these polymers. U.S. Patent 5,369,142 to Culbertson and Kao, and Kao *et al.*, Dent. Mater *12*:44-51 (1996), teach ionomeric glass cement compositions wherein the copolymer is modified to

30 include an amino acid *e.g.*, N-acryloyl substituted amino acid. *Kao* found increases in diametral tensile, compressive and/or flexural strengths and fracture toughness in cements in which the co-polymer contained an amino acid.

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Despite these improvements, however, there remains a need for orthopaedic and dental cements that are stronger and exhibit greater working time in which to allow dental practitioners and orthopaedic surgeons to work with them.

5   SUMMARY OF THE INVENTION

One aspect of the present invention is directed to a composition for making an ionomeric cement. The composition contains at least one copolymer containing at least two different carboxylic acid-containing monomers, wherein the copolymer has pendent polymerizable functional groups, and a comonomer containing one or more functional groups reactive with the polymerizable functional groups. The comonomer, at least one of the carboxylic acid containing monomers, or both, contains an amino acid moiety. In preferred embodiments, the copolymer contains three carboxylic acid monomers, two of which are acrylic acid and itaconic acid, and the third monomer is an acryloyl- or methacryloyl derivative of beta-alanine, glycine, aspartic acid, glutamic acid, 6-aminocaproic acid or methionine.

20   Another aspect of the present invention is directed to an ionomeric cement composition. The cement composition contains, in addition to the copolymer and comonomer, a reactive filler and water.

A further aspect of the present invention is directed to a polymerization system, *per se*. The system contains at least one copolymer containing at least two different carboxylic acid-containing monomers, wherein the copolymer has pendent polymerizable functional groups, and a comonomer containing one or more groups reactive with the polymerizable functional group. At least one of the monomers, the comonomer or both contains an amino acid moiety.

Yet another aspect of the present invention is directed to a kit that contains at least one package containing various of the ingredients necessary to prepare the ionomeric cement

compositions. In preferred embodiments wherein the cement is ultimately prepared using a redox polymerization initiation system, one package contains the reactive filler and the reducing agent (preferably in microencapsulated form), and

5 another package contains the copolymer, comonomer, oxidizing agent and water. In other embodiments a first package contains the reactive filler, copolymer and comonomer, and the second package contains water. If a redox system is used, the first package may also contain the reducing agent and the

10 second package may contain the oxidizing agent. The reducing agent and the oxidizing agent may be in either package. Methods of making and using the cements are also provided.

Ionomeric cement compositions of the present invention are non-biodegradable; they form a rigid hydro-gel that can be

15 loaded with bioactive agents for release over extended periods of time. They exhibit superior biocompatibility, hydrophilicity, reduced cytotoxicity; very low polymerization shrinkage and exotherm; self-healing characteristics in that ionic cross-links that break due to mechanical forces may

20 reform over time; and they exhibit longer working time and stronger and more durable chemical bonding to bone and metal alloys.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a flow diagram of a "one-pot" synthesis of a

25 terpolymer grafted with isocyanatoethyl methacrylate(IEM), according to the present invention.

Fig. 2 is a bar graph illustrating compressive strengths of ionomeric cements of the present invention having pendent vinyl groups from IEM graft and polymerized via photo-

30 initiation.

Fig. 3 is a bar graph illustrating flexural and diametral tensile strengths of ionomeric cements of the present invention having pendent vinyl groups from IEM graft and polymerized via photo-initiation.

5   Fig. 4 is a bar graph illustrating compressive and diametral tensile strengths of ionomeric cements of the present invention having pendent vinyl groups from IEM graft and polymerized via redox-initiation.

Fig. 5 is a bar graph illustrating flexural and diametral

10   tensile strengths of ionomeric cements of the present invention having pendent vinyl groups obtained through glycydol methacrylate (GM) grafting and polymerized via redox-initiation.

Fig. 6 is a bar graph illustrating compressive strengths

15   and viscosities of ionomeric cements of the present invention having pendent vinyl groups from IEM grafted and polymerized via photo-initiation, using different vinyl-containing monomers as a comonomer including amino acids, acrylic acid, and HEMA, wherein HEMA = 2-hydroxyethyl methacrylate; MASPA =

20   methacryloyl aspartic acid; AGA = acryloyl glutamic acid; ABA = acryloyl beta-alanine; MGA = methacryloyl glutamic acid; MBA = methacryloyl beta-alanine; AASPA = acryloyl aspartic acid; and AA = acrylic acid.

Fig. 7 is a graph illustrating compressive strengths and

25   viscosities of ionomeric cements of the present invention having pendent vinyl groups from IEM grafted and polymerized via photo-initiation, with different formulations of IEM grafted terpolymer / methacryloyl beta-alanine / water.

Fig. 8 is a bar graph illustrating compressive strengths

30   of ionomeric cements of the present invention having pendent vinyl groups from IEM grafted and polymerized via photo-initiation, at different powder/liquid ratios, using methacryloyl beta-alanine as a comonomer.

Fig. 9 is a bar graph illustrating compressive, diametral tensile and flexural strengths of ionomeric cements of the present invention having pendent vinyl groups from IEM grafted and polymerized via photo-initiation, as compared to a commercial GC Fuji II LC glass-ionomer cement.

DETAILED DESCRIPTION

The term "ionomer" refers to a polymer or copolymer having sufficient pendent ionic groups to undergo a setting reaction or curing reaction in the presence of a reactive filler material and water. Water serves as a reaction medium facilitating the transport of ions between the ionomer and the filler, thereby allowing the acid-base chemical cure setting reaction to occur.

By the term "reactive filler", it is meant a powdered or otherwise surface-active metal oxide or hydroxide, mineral silicate, or ion leachable glass or ceramic, that is capable of reacting with the ionomer in the presence of water to form a hydrogel. Representative examples of reactive filler materials include calcium-containing and aluminum-containing materials such as calcium alumino silicate glass, calcium alumino fluorosilicate glass, calcium aluminum fluoroborosilicate glass, and like materials known in the art of glass-ionomer cements. In embodiments wherein the cement is used for dental purposes, reactive powders that contain leachable fluorides may be beneficial from the standpoint of cariostatic prevention. Examples of such powders are fluoroaluminosilicate and fluoroaluminoborate ion-leachable glasses.

Polymerizable acids used for preparing ionomers useful for glass-ionomer cement systems include alkenoic acids and unsaturated mono-, di- and tricarboxylic acids. Representative alkenoic acids are described, for example, in U.S. Patents 3,655,605; 4,016,124; 4,089,830; 4,143,018; 4,342,677; 4,360,605; 4,376,835 and 5,130,347. Specific

examples are acrylic acid, maleic acid, fumaric acid, itaconic acid, crotonic acid, methacrylic acid, the acid chlorides thereof and the acid anhydrides thereof and chloro or bromo derivatives thereof. Particularly preferred monomers are

5   acrylic acid(AA), itaconic acid (IA) and maleic acid (MA), and the chlorides or anhydrides thereof.

The incorporation of naturally occurring amino acids to glass-ionomer bone cements of the present invention promotes biocompatability and enhances mechanical properties. In

10   addition, their incorporation leads to better handling characteristics at higher molecular weight compared to poly (acrylic) acid homopolymers or acrylic acid/itaconic acid copolymers. The amino acid-containing monomer that is used in the present invention may be naturally occurring or synthetic

15   in nature. Examples are glycine, glycylglycine, alanine, valine, leucine, isoleucine, phenylalanine, tyrosine, proline, hydroxyproline, serine, threonine, 3-amino-3-methylbutanoic acid, 6-aminocaproic acid, aminobenzoic acid (meta and para), 4-aminosalicylic acid, iminodiacetic acid, lanthionine,

20   methionine, aspartic acid, glutamic acid, lysine, delta-aminolevulinic acid, beta-alanine, alpha-aminobutyric acid, gamma-aminobutyric acid, gamma, epsilon-diaminopimelic acid, gamma, alpha-diaminobutyric acid, ornithine, omega-aminododecanoic acid, beta-cyanoalanine, epsilon-

25   methylhistidine, canavanine, djenkoic acid, 1-azaserine, gamma-methylene glutamic acid, N-methyl tyrosine, arginine, tryptophan, norvaline, cystine, cysteine, and hydroxylysine.

Preferred amino acids contain acryloyl or methacryoyl groups. Specific examples include acryloyl beta-alanine

30   (ABA), acryloyl glycine (AG), acryloyl aspartic acid(AASPA), acryloyl glutamic acid (AGA), acryloyl 6-aminocaproic acid (AbACA, methacryloyl beta-alanine (MBA), methacryloyl glycine (MG), methacryloyl aspartic acid (MASPA), methacryloyl glutamic acid (MGA) and methacryloyl 6-aminocaproic acid

(M6ACA)and methacryloyl methionine (MMET).   The many other
polypeptide fragments known to those skilled in the art may
also be treated according to the present invention with
acryloyl or methacryloyl acid chloride or anhydride to produce
5   new monomers suitable for the polymers in the cements of the
present invention. For example, the dimer of glutamic acid,
glycine-glutamic acid peptide unit, etc., reaction with
acryloyl chloride would produce a monomer having high acid and
amide group content and thereby be useful herein.   The
10 acryloyl or methacryloyl derivatives of amino acids are
prepared by known synthetic techniques.   See, for example,
U.S. Patent 5,369,142 to Culbertson, and Kao *et al.*, Dent.
Mater *12*:44-51 (1996).

Preferred copolymers of the present invention are
15 terpolymers having the following formula: Poly(AA-IA-AGA);
Poly(AA-IA-MGA); Poly(AA-IA-AG); Poly(AA-IA-MG); Poly(AA-IA-
ABA); Poly(AA-IA-MBA); Poly(AA-IA-A6ACA); and Poly(AA-IA-
M6ACA). In some embodiments of the present invention, the
cement composition contains two or more such copolymers.
20 Preferred combinations include blends of Poly (AA-IA-
MGA)/Poly(IA-IA-M6ACA), Poly(AA-IA-MGA)/Poly(AA-IA-MG) and
Poly(AA-IA-AASPA)/Poly(AA-IA-MG). The relative amounts of
copolymers range from about 10% to about 90% by total weight
of copolymers. In preferred embodiments, the copolymers are
25 present in roughly equal amounts, *e.g.*, each about 50% by
weight. In other embodiments, the cement contains at least
one additional polymer or copolymer known in the art *e.g.*,
poly AA, poly IA, copolymers of AA and IA, etc. The addition
of these elements may improve toughness and decrease
30 brittleness of the ultimate cement composition.

The pendent carboxylic acid groups on the copolymer must
be sufficient in number or percent by weight to bring about
the setting or curing reaction in the presence of the reactive

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powder.   To create a source of additional covalent cross-
linking, which imparts additional strength to the ultimate
ionomeric cement composition, a portion of the carboxylic acid
groups is reacted with a bi-functional monomer.   Suitable bi-
5   functional monomers are water soluble and undergo a reaction
with a carboxylic acid group to form a covalent bond, while
maintaining a polymerizable functional group capable of
addition polymerization.   Thus, one functionality of this
monomer facilitates grafting on to the copolymer backbone via
10   the carboxylic acid groups.   In preferred embodiments, such
functionalities contain nucleophilic groups such as hydroxyl,
amine, isocyanato and epoxy.   The other functionality is a
polymerizable functional group capable of addition
polymerization.   Preferred polymerizable functional groups
15   include ethylenically unsaturated groups such as vinyl groups,
and epoxy groups.   In other preferred embodiments, the bi-
functional monomer further contains at least one carboxyl or
hydroxyl group to enhance water solubility of the copolymer.
Examples of suitable bi-functional monomers include acryloyl
20   chloride, methacryloyl chloride, vinyl azalactone, allyl
isocyanate,   2-hydroxyethylmethacrylate   (HEMA),   2-
aminoethylmethacrylate, 2-isocyanatoethyl methacrylate (IEM),
acrylic acid, methacrylic acid and N-vinylpyrrolidone.   Other
examples of suitable bi- functional monomers are described in
25   U.S. Patent 4,035,321 and on columns 5-7 of U.S. Patent
5,130,347 to Mitra.   Preferred bi-functional monomers are the
amino acid-containing monomers described herein, GM, IEM and
HEMA.   In general, the bi-functional monomer is present in an
amount of from about 5 to about 50%, and preferably from about
30   10 to about 25%, based upon the mole fractions of the
copolymer and the bi-functional monomer.

        To effect the additional cross-linking of the cement, one
or more comonomers are included in the cement composition.
The comonomer contains at least one polymerizable functional

group reactive with the polymerizable functional groups on the copolymer backbone (provided by the bifunctional monomer). Suitable polymerizable functional groups in the comonomers include but are not limited to ethylenically unsaturated

5 groups (e.g., alkenyl groups and preferably vinyl groups) and epoxy groups. Ethylenically unsaturated groups, especially those that can be polymerized by means of a free radical mechanism e.g., substituted and unsubstituted acrylates, methacrylates, alkenes and acrylamides, are preferred. In

10 aqueous systems, polymerizable groups that are polymerized by a cationic mechanism e.g., polymerizable ethylenically unsaturated groups such as vinyl ether groups and polymerizable epoxy groups, are less preferred since a free radical mechanism is typically easier to employ in such

15 systems than a cationic mechanism. Preferred comonomers include the amino acid-containing monomers described herein. More preferred comonomers are acryloyl beta-alanine, methacryloyl beta-alanine, acryloyl glutamic acid and methacryloyl glutamic acid. In general, the comonomer is

20 present in the ultimate cement composition in an amount of from about 10% to about 60%, preferably from about 15 to about 50%, and more preferably from about 20 to about 35%, based upon the total weight of the total copolymer/comonomer/water mixture.

25   Methods for preparing the ionomeric copolymers e.g., via free-radical polymerization, are well known. (See, Crisp et al., "Glass ionomer cement formulations. II. The synthesis of novel polycarboxylic acids," in J. Dent. Res. 59(6):1055-1063 (1980)). In preferred embodiments, the ionomeric copolymer is

30 prepared first and then the polymerizable functional groups are added (e.g., grafted thereon). This sequence substantially eliminates integration of the functional groups into the copolymer backbone. General procedures of grafting

pendent polymerizable groups onto the ionomeric copolymers are known in the art *e.g.*, U.S. Patent 5,130,347.

The relative proportions of monomers and comonomer vary depending upon the desired properties of the cement *e.g.*,
5   orthopaedic or dental. In embodiments wherein the amino acid containing monomer is part of the copolymer backbone, the molar ratio of the total amount of other monomer(s) to the amino acid ranges from about 7:1 to about 11:1. In preferred embodiments of the present invention wherein the copolymer
10 contains acrylic acid, itaconic acid and an amino acid, preferably an acryloyl- or methacryloyl amino acid, molar ratios of acrylic acid to itaconic acid to amino acid range from about 10:1:1 to about 5:2:1, and more preferably about 8:2:1 respectively. Likewise, the number average molecular
15 weight (Mn) generally varies from about 3,500 to about 110,000 daltons, and preferably from about 5,500 to about 80,000 daltons.

To prepare the ionomeric cement, the copolymer is mixed with the reactive powder and the comonomer in the presence of
20 water. The components of the ionomeric cement system can be combined (such as by mixing or blending) in a variety of manners and amounts in order to form the ionomeric cements of this invention. Suitable combining techniques include those commonly employed to mix ionomer cement systems. In one
25 technique, a concentrated aqueous solution of the copolymer and comonomer (*i.e.*, ionomer) is mixed with reactive powder at the time of use. The resultant combination of ionomer, reactive powder and water allows the setting reaction to begin. In another technique, the ionomer and powder are
30 provided as a freeze-dried or lyophilized powdered blend under substantially anhydrous conditions *i.e.*, conditions in which there is not sufficient water to allow the setting reaction to proceed. Such systems can then be combined with water at the

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time of use in order to begin the setting reaction. Once the
setting reaction has begun, the resultant mixture may be
formed into its desired shape, followed by curing and allowing
the mixture to fully harden.

5   In general, the weight-to-weight ratio of the
copolymer(s) to water is from about 1:9 to about 9:1. In
general, the concentration of copolymer in water ranges from
about 30 to about 70% by weight, and preferably from about 40
to about 65 percent. The resultant aqueous solution has a
10   ratio of polymer to liquid generally ranging from about 1.5 to
about 8.

          In addition to the particular polymerization initiation
system, the reaction mixture may also include a modifying
agent such as tartaric acid, thereby providing the ability to
15   achieve a longer working time and a shorter setting time,
respectively, when preparing the cement. The term "working
time" is generally regarded as referring to the time between
the beginning of the setting reaction when the ionomer and
reactive powder are combined in the presence of water, and the
20   time the setting reaction proceeds to the point when it is no
longer practical to perform further physical work upon the
system, e.g. spatulate it or reshape it, for its intended
dental or medical application. The term "setting time" refers
to the time measured from the beginning of the setting
25   reaction in a restoration to the time sufficient hardening has
occurred to allow subsequent clinical or surgical procedures
to be performed on the surface of the restoration. In the
setting reaction, the reactive filler behaves like a base and
reacts with the acidic ionomer to form a metal polysalt which
30   acts as the binding matrix. The setting reaction is therefore
characterized as a chemical cure system that proceeds
automatically upon mixing the ionomer and reactive filler
material in the presence of water. The cement sets to a gel-
like state within a few minutes and rapidly hardens to develop

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strength. See *e.g.*, Prosser *et al.*, J. Chem. Tech. Biotechnol. *29*:69-87 (1979). Tartaric acid and other chelating agents have proven useful in modifying the setting rate such as to provide longer working times for the cements.

5 See *e.g.*, U.S. Patents 4,089,830, 4,209,434, 4,317,681 and 4,374,936. In general, an increase in working time results in an increase in setting time as well.

The ratio of powder (*i.e.*, reactive powder or powdered blend of ionomer and reactive powder) to liquid affects the

10 workability of the mixed ionomer cement systems. Ratios higher than about twenty to one (powder to liquid, by weight) tend to exhibit poor workability, while ratios below about one to one tend to exhibit poor mechanical properties, *e.g.*, strength, and hence are not preferred. Preferred ratios are on the order

15 of about 1:3 to about 6:1 and preferably about 1:1 to 4:1 for the reactive powder (*i.e.*, glass plus reducing agent) to liquid system, (copolymer, comonomer and water) and about 1:1 to 16:1 and preferably about 4:1 to 14:1 for the powdered blend system (*i.e.*, glass, reducing agent, copolymer and

20 comonomer). Higher glass (*i.e.*, powder) contents lead to materials with higher compressive strengths, while lower glass contents lead to materials with high flexural strengths and toughness.

Other ingredients, such as polymerization initiators,

25 modifying agents and co-solvents can be added at any time and in any manner that does not prematurely begin the setting reaction or the photo-curing reaction. Modifying agents can be used in the ionomer cement systems of the present invention in order to provide prolonged working times.

30 The cements are polymerized in accordance with known techniques. At least one initiator is required for most polymerization methods such as those based on oxidation/reduction reactions and ultraviolet and visible

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light.   Photo-initiators promote free radical cross-linking of
the ethylenically unsaturated component on exposure to light
of a suitable wavelength and intensity.   It should also be
sufficiently shelf-stable and free of undesirable coloration
5   to permit storage and use under typical medical or dental
conditions.   The photo-initiator preferably is water-soluble
or water-miscible.   Photo-initiators bearing polar groups
usually possess a sufficient degree of water-solubility or
water-miscibility to qualify for this use.   The photo-
10   initiator can be used alone but it may be used in combination
with a suitable donor compound or accelerator (e.g., amines,
peroxides, phosphorus compounds, ketones and alpha-diketone
compounds).   Preferred visible light-induced initiators
include camphoroquinone (which typically is combined with a
15   suitable hydrogen donor such as an amine), diaryliodonium
simple or metal complex salts, chromophore-substituted
halomethyl-s-triazines and halomethyl oxadiazoles.
Particularly preferred visible light-induced photo-initiators
include combinations of an alpha-diketone e.g.,
20   camphoroquinone, and a diaryliodonium salt, e.g.,
diphenyliodonium chloride, bromide, iodide or
hexafluorophosphate, with or without additional hydrogen
donors (such as sodium benzene sulfinate, amines and amine
alcohols).   Preferred ultraviolet light-induced polymerization
25   initiators include ketones such as benzyl and benzoin, and
acyloins and acyloin ethers.
        The photo-initiator should be present in an amount
sufficient to provide the desired rate of photo-
polymerization. The amount depends on factors including the
30   light source, the thickness of the cement layer to be exposed
to radiant energy and the extinction coefficient of the photo-
initiator.   In general, the photo-initiator components are
present at a total weight of about 0.01 to about 5%,

preferably from about 0.1 to about 5%, based on the total weight (including water) of the unset cement components.

Initiation of polymerization based on oxidation/reduction ("redox") reactions entails the reaction or cooperation

5   between a reducing agent and an oxidizing agent to produce free radicals that in turn initiate polymerization of the pendant functional groups on the ionomeric copolymer. Like photo-initiators, redox reagents exhibit adequate storage stability and lack of colorization under typical conditions of

10   use. In addition, they should be sufficiently water-soluble to permit ready dissolution in (and discourage separation from) the other components of the cement. They are present in an amount sufficient to permit an adequate free-radical reaction rate. In general, these amounts range from about 0.01

15   to about 10%, and preferably from about 0.02 to about 5%, based on the total weight (including water) of the unset cement components.

Reducing agents (also termed "activators") include ascorbic acid, cobalt (II) chloride, ferrous chloride, ferrous

20   sulfate, hydrazine, hydroxylamine (depending upon the choice of oxidizing agent) oxalic acid, thiourea, and salts of a dithionite or sulfite anion. Preferred reducing agents include ascorbic acid and ferrous sulfate. Oxidizing agents (also termed "initiators") include cobalt (III) chloride,

25   tert-butyl hydroperoxide, ferric chloride, hydroxylamine (depending upon the choice of reducing agent), perboric acid and its salts, and salts of a permanganate or persulfate anion. Preferred oxidizing agents are potassium persulfate, ammonium persulfate and hydrogen peroxide.

30   Microencapsulation of the reducing agent enhances storage stability and allows the reducing agent and oxidizing agent to be packaged together. Water-soluble and water-insoluble encapsulants can be employed; water-insoluble encapsulants are preferred because they generally provide better long-term

storage stability under moist or humid conditions. Suitable encapsulating materials include cellulosic materials as cellulose acetate, cellulose acetate butyrate, ethyl cellulose, hydroxymethyl cellulose and hydroxyethyl cellulose

5   being preferred. Other encapsulants include polystyrene, copolymers of polystyrene with other vinylic monomers and polymethylmethacrylate, copolymers of methylmethacrylate with other ethylenically-unsaturated monomers. Preferred encapsulants are ethylcellulose (EC) and cellulose acetate

10   butyrate (CAB). By varying the choice of encapsulant and the encapsulation conditions, the onset of curing can be tailored to start at times ranging from seconds to minutes. Additional optimization of the encapsulation process allows the mixing and setting times to be customized to a delivery system or to

15   the needs of a specific clinical procedure. The ratio of amount of encapsulant to activator generally ranges from 0.5 to about 10 and preferably from about 2 to about 6.

Typically, the copolymer(s) and comonomer are packaged together. Depending upon the application of the cement and

20   the manner in which polymerization is achieved, various components of the cement compositions may be packaged differently. For example, in the case of a redox-based system, ingredients of the cement composition are divided into two separate packages -- the first package containing the

25   copolymer, comonomer, the initiator (*i.e.*, oxidizing agent) and water, and the second package containing the reactive filler and the activator (*i.e.*, the reducing agent). In another embodiment, the first package contains all solid materials (*e.g.*, copolymer, comonomer, reactive filler and if

30   desired, the reducing agent, and the second package contains water and if desired, the initiator. In the case of photo-initiation, the photo-initiator can be included in either the solid (*e.g.* paste) or liquid parts of the cement.

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        The cements of the present invention may further contain
pigments, nonvitreous fillers, polymerization inhibitors e.g.,
hydroxytoluene, free radical scavengers e.g., 4-methoxyphenol,
butylated hydroxytoluene (BHT), reactive and nonreactive
5   diluents e.g., 2-hydroxyethyl methacrylate, hydroxypropyl
methacrylate, surfactants (such as to enhance solubility of an
inhibitor e.g., polyoxyethylene) and coupling agents to
enhance reactivity of fillers e.g., 3-(trimethoxysilyl)propyl
methacrylate. The amount of inhibitor added ranges from about
10 0.001 to about 2% and preferably from about 0.02 to about 0.5%
based on the total weight of the copolymer/comonomer/water
mixture. BHT is a preferred inhibitor. It is employed in
conjunction with a surfactant (in an amount of about 1%) to
enhance solubility.

15   The cements of the present invention can be used in a
variety of applications in the dental and medical fields.
Dental applications include restoratives for lining or basing,
cementation, sealants and as adhesives and bulk filling.
Orthopaedic applications include cements for prosthetic joint
20 (e.g., knee and hip) replacement, bone grafts, and repair of
bony defects from disease or trauma.

        The invention will now be illustrated by way of the
following examples. They are not intended to limit the scope
of the presently disclosed invention in any way. Unless
25 indicated otherwise, all parts are by weight.

EXAMPLE 1

Synthesis of methacryloyl L-glutamic acid (MGA)

        NaOH (60 g, 1.5 mol) was dissolved in 250 ml of water and
cooled down to around 15°C. L-Glutamic acid (73.6 g, 0.5 mol)
30 was then dissolved in the NaOH aqueous solution. To a three-
neck flask, equipped with a thermometer and a mechanical
stirrer, containing L-glutamic acid and NaOH aqueous solution,
and cooled down to 0 to 5°C, methacryloyl chloride (48.9 ml,

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0.5 mol) was added dropwise with vigorous stirring within about one hour while keeping the temperature below 5°C. An additional hour was allowed to complete the reaction after the addition was completed. The solution was acidified to pH = 2

5   with a solution of concentrated HCl (37%) and distilled water (1:1, v/v), oversaturated with NaCl at room temperature, and extracted three to four times with warm ethyl acetate (50 – 60°C). The extracted solution was separated using a separation funnel, dried with anhydrous $MgSO_4$, filtered with a

10 Buchner funnel, and concentrated using a rotary vacuum evaporator to obtain white crystals. The rectangular and transparent crystals were obtained by recrystallization from ethyl acetate.
EXAMPLE 2

15 Synthesis of methacryloyl glycine (MG)
    The same procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with glycine (37.5g, 0.5 mol), NaOH (40g, 1.0 mol), water (250 ml), and methacryloyl chloride (48.9 ml, 0.5 mol) to yield a white

20 crystalline material. Needle-like and transparent crystals were obtained after recrystallization from warm ethyl acetate (50 – 60°C).
EXAMPLE 3
Synthesis of methacryloyl L-aspartic acid (MASPA)

25 A similar procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with L-aspartic acid (66.6g, 0.5 mol), NaOH (60g, 1.5 mol), water (250 ml), and methacryloyl chloride (48.9 ml, 0.5 mol) to yield a white slurry and viscous material. After being refrigerated

30 overnight, white crystals precipitated out of the slurry material. The white crystals were dried under vacuum at 25°C after washed using hexane.
EXAMPLE 4

Synthesis of methacryloyl beta-alanine (MBA)

A similar procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with beta-alanine (44.5 g, 0.5 mol), NaOH (40 g, 1.0 mol), water (250 ml), and
5 methacryloyl chloride (48.9 ml, 0.5 mol) to yield a white crystalline material, which was dried under vacuum at 25°C after being washed with hexane.

EXAMPLE 5

Synthesis of methacryloyl 6-aminocaproic acid (M6ACA)
10 A similar procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with 6-aminocaproic acid (65.6g, 0.5 mol), NaOH (40g, 1.0 mol), water (250 ml), and methacryloyl chloride (48.9 ml, 0.5 mol) to yield a light yellow oily organic material. After being refrigerated
15 overnight, light yellow crystals precipitated out of the oily material. The yellowish crystals were dried under vacuum at 25°C.

EXAMPLE 6

Synthesis of methacryloyl D,L-methionine (MMET)
20 A similar procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with D,L-methionine (74.6g, 0.5 mol), NaOH (40g, 1.0 mol), water (250 ml), and methacryloyl chloride (48.9 ml, 0.5 mol) to yield a light yellow, slightly odiferous crystalline material which was
25 dried under vacuum at 25°C.

EXAMPLE 7

Synthesis of acryloyl L-glutamic acid (AGA)

The same procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with L-glutamic
30 acid (147.1 g, 1.0 mol), NaOH (120 g, 3.0 mol), water (350 ml), and acryloyl chloride (81.3 ml, 1.0 mol) to yield a white crystalline material. Cubic and transparent crystals were obtained after recrystallization from warm ethyl acetate (50 – 60°C) and drying under vacuum at 25°C.

EXAMPLE 8

Synthesis of acryloyl glycine (AG)

The same procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with glycine (75.1 g, 1.0 mol), NaOH (80 g, 2.0 mol), water (350 ml), and acryloyl chloride (81.3 ml, 1.0 mol) to yield a white crystalline material. Cubic and transparent crystals were obtained after recrystallization from warm ethyl acetate (50 – 60°C) and drying under vacuum at 25°C.

EXAMPLE 9

Synthesis of acryloyl L-aspartic acid (AASPA)

The similar procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with L-aspartic acid (133.1g, 1.0 mol), NaOH (120g, 3.0 mol), water (350 ml), and acryloyl chloride (81.3 ml, 1.0 mol) to yield a white slurry and viscous material. After being refrigerated overnight, white crystals precipitated out of the slurry material. The white crystals were dried under vacuum at 25°C after being washed with hexane.

EXAMPLE 10

Synthesis of acryloyl beta-alanine (ABA)

The same procedure, as described in synthesis of methacryloyl L-glutamic acid, was utilized with beta-alanine (89.1g, 1.0 mol), NaOH (80g, 2.0 mol), water (350 ml), and acryloyl chloride (81.3 ml, 1.0 mol) to yield a white crystalline material, which was dried under vacuum at 25°C after washing with hexane.

EXAMPLE 11

Synthesis of acryloyl 6-aminocaproic acid (A6ACA)

The general procedure was similar to that described in synthesis of methacryloyl L-glutamic acid. To an aqueous solution of 6-aminocaproic acid (131.2g, 1.0 mol), NaOH (80g, 2.0 mol), and water (350 ml), acryloyl chloride (81.3 ml, 1.0 mol) was added dropwise for about one and one half hours.

After reaction was complete, the solution was acidified to pH = 2 with a solution of concentrated HCl (37%) and distilled water (1:1, v/v), and oversaturated with NaCl at room temperature. The white slurry and crystalline materials were
5   extracted three to four times with warm ethyl acetate (50 - 60°C). The extracted solution was separated using a separation funnel, dried with anhydrous $MgSO_4$, filtered with a Buchner funnel, and concentrated using a rotary vacuum evaporator to obtain white fine crystals. These fine crystals
10   were dried under vacuum at 25°C.

Yield and melting point of the synthesized monomers in Examples 1-11 are shown in Table 1.

Table 1. Yield and Melting Point of the Monomers

Code	Yield (%)	Melting Point (°C)
AGA	34 - 38	116 - 118
MGA	48 - 55	128 - 130
AG	33 - 35	128 - 130
MG	55 - 68	104 - 105
ABA	46	84 - 86
MBA	62	66 - 69
A6ACA	92	72 - 76
M6ACA	76	87 - 90
AASPA	25	135-138
MASPA	56	93 - 96
MMET	44	71 - 72

15   EXAMPLE 12

One-Pot Synthesis of Poly(Acrylic Acid-co-Itaconic Acid-co-Methacryloyl Glutamic Acid) with Pendent 2-Isocyanatoethyl Methacrylate (IEM)

The general reaction scheme is illustrated in Fig. 1. To
20   a three-neck flask, equipped with a thermometer, a nitrogen inlet, a condenser, a drop funnel and a mechanical stirrer, containing 2,2'-azobisisobutyronitrile (AIBN) (0.2645g) and 125 ml of tetrahydrofuran (THF), a liquid mixture of AIBN (0.2625 g), acrylic acid (AA), (27.38 ml), itaconic acid (IA)
25   (12.99 g) and methacryloyl glutamic acid MGA (10.74 g) and 150

ml of THF were added in about one hour.   Before the reaction
was initiated, the system was purged with N_2 for 30 min. to
displace the dissolved oxygen and then the temperature was
raised to around 62-64°C. Nitrogen purging was continued until

5   the reaction was completed.   After completion of the
additions, the polymerization was run for an additional 10 -
12 hours at the same temperature.   The molar feed ratio for
the terpolymer was 8:2:1 (AA: IA: MGA).

The above solution was then cooled down to 35-40°C and

10 kept at this temperature until the reaction was completed.   To
the solution, 0.09g of butylated hydroxy-toluene (BHT), 0.09g
of triphenylstibine (TPS) and 0.6g of dibutyltin dilaurate
(DBTL) were added.   After the solution became clear, a mixture
of 27.07g of IEM and 27 ml of THF were added dropwise within

15 1.5 hours.   Another two-hour period was used to complete the
reaction.   Both FTIR (Fourier transform-infrared spectroscopy)
and ^{1}H-NMR (proton nuclear magnetic resonance spectroscopy)
were used to monitor the reaction.

The terpolymer grafted with IEM was recovered by

20 precipitation from diethyl ether, followed by drying in a
vacuum oven at room temperature.

The grafted terpolymer was characterized by FT-IR (NMR).
The FT-IR spectra were obtained with a FT-IR Spectrometer
(Model 1600 FTIR, The Perkin Elmer Co., Norwalk, CT), where

25 the sample film was cast on the NaCl crystal. ^{1}H NMR spectra
were obtained on a Bruker AM 400 MHz NMR spectrometer using
deuterated dimethylsulfoxide as solvent.
EXAMPLE 13
One-Pot Synthesis of Poly(Acrylic Acid-co-Itaconic Acid) with

30 Pendent Glycidyl Methacrylate (GM)

The same procedure, as described in the synthesis of
poly(acrylic acid-co-itaconic acid-co-methacryloyl glutamic
acid), was used to produce the poly(acrylic acid-co-itaconic
acid) copolymer with the molar feed ratio of 7:3.

24

The formed solution was then cooled down to around 62°C and kept until reaction was completed. To the solution, 1.05 g of BHT and 3.15 g of N,N-dimethylaniline (DMA) were added. After the solution became clear, a mixture of 30.0g of GM and

5   30 ml of THF were added dropwise within about 1.5 hours. Another 30-hour period was used to complete the reaction. Both FTIR and ^{1}NMR were used to trace the reaction. The copolymer grafted with GM was recovered by precipitation from diethyl ether, followed by drying in a vacuum oven at

10   room temperature.

The grafted terpolymer was identified by FT-IR and nuclear magnetic resonance (NMR). The FT-IR spectra were obtained with a FT-IR Spectrometer, where the sample film was cast on the NaCl crystal. ^{1}H NMR spectra were obtained on a

15   Bruker AM 400 MHz NMR spectrometer using deuterated dimethyl-sulfoxide as a solvent.

EXAMPLE 14

One-Pot Synthesis of Poly(Acrylic Acid-co-Itaconic Acid-co-Methacryloyl Glutamic Acid) with Pendent Glycidyl Methacrylate

20   (GM)

A similar procedure, as described in Example 12 for synthesis of poly(acrylic acid-co-itaconic acid-co-methacryloyl glutamic acid) with the molar feed ratio of 8:2:1 and in Example 13 for GM grafting, was used to produce the

25   desired terpolymer with pendent vinyl functionality.

EXAMPLE 15

Microencapsulation of Ascorbic Acid in Cellulose Acetate Butyrate (CAB)

Into a round bottom flask containing 150 ml of ethyl

30   acetate, 2.0g of cellulose acetate butyrate (CAB, MW = 200,000, butyrate content = 17%) was added and dissolved for about 2-3 hours to form a homogenous solution. A water bath was placed under the flask for cooling later. Then 1.0g of ascorbic acid was added and suspended in the solution for

about 15 to 30 minutes, with stirring. 150-200 ml of n-hexane
was added dropwise at the rate of 80-100 drops per min. After
completion of addition of n-hexane, ice water was added into
the bath to harden the formed microcapsules. After 5-10
5   minutes, cold n-hexane was added to wash the microcapsules.
The microcapsules were recovered by decantation, washed with
cold n-hexane, and air-dried or vacuum-dried.

EXAMPLE 16
Formulation and. Preparation of Vinyl-Containing Hybrid Glass-
10   Ionomer Bone Cements Using Redox Initiators
        A two-component system (liquid and solid) was used for
formulating redox initiator containing hybrid glass-ionomer
cements. The liquid component containing an oxidizer was made
by mixing vinyl containing terpolymer (40-60% of total liquid,
15   wt %) with $K_2S_2O_8$ (0.1-0.5%), butylated hydroxytoluene (BHT,
0.2-0.8%), polyoxyethylene nonylphenol (PEONP, 0.6%), vinyl-
containing amino acid (20-30%) and distilled water (15-30%).
The solid component containing a reducing agent was prepared
by mixing GC Fuji II LC™ glass powder (GC American Dental Co.)
20   with ascorbic acid containing microcapsules (0.2-0.6% of glass
powder, wt %), using a vortex with a maximal speed. A
powder/liquid ratio (P/L) of 1.0-2.5/1 was used in the
formulation. A typical formulation is shown in Table 2.

Table 2. Two-Component Redox Glass-Ionomer Bone Cement

	Powder	Liquid
Composition	Commercial Fuji II LC glass (GC America) *ascorbic acid, encapsulated with cellulose acetate butyrate, 0.4 % of glass (wt %). *Ratio of ascorbic acid/cellulose acetate butyrate = 1/3 (wt/wt).	50 (wt %) Poly(acrylic acid-co-itaconic acid-co-glutamic acid) grafted with 15 % 2-isocyanatoethyl methacrylate (mol % of polyacid). 18 (wt %) Acryloyl beta-alanine (comonomer) 32 (wt %) Distilled water

	0.1 (wt %) $K_2S_2O_8$
	0.2 (wt %) Butylated hydroxytoluene (inhibitor)
	0.6 (wt %) Polyoxyethylene nonylphenol
P/L ratio 2-2.5 (wt/wt)	1

EXAMPLE 17

Estimates of Curing Time of the Redox System

       A metal rod was used to evaluate the working time. The
rod was inserted into the center of a mixture of the cement,
which was mixed and packed into a small vial with a hole at
the bottom. Working time was recorded once the mixing process
was initiated. The moment at which the metal rod could not be
manually moved in the cement measured from the time of mixing,
is defined as the working time. The working times estimated
are shown in Table 3.

Table 3. Working Time of Self-Cured Hybrid GI Bone Cement*

Code	Encapsulant	Ratio (ascorbic acid vs. encapsulant, wt/wt)	Working Time (min, observed)
XMG1	ethyl cellulose	1:1	1
XMG2	ethyl cellulose	1:2	2
XMG3	ethyl cellulose	1:3	2-3.5
XMG4	cellulose acetate butyrate	1:2	4-5
XMG5	cellulose acetate butyrate	1:3	5-6

*Fuji II LC glass was used to make formulations. The polymer
liquid was made in formulation of 50/20/30 (grafted
terpolymer/ABA/water).

EXAMPLE 18a

Specimen Preparation Using Redox Initiators

       Polymer solutions were made as described in example 15.
GC Fuji II LC^{TM} glass powder was supplied by GC American
Dental Co. and used in accordance with manufacturer's

instructions.   The glass powder versus polymer liquid (P/L) ratio was in the range of 1.5 to 2.5.

Specimens were mixed and fabricated at room temperature, according to manufacturer's instructions.   The cylindrical

5   specimens were prepared in molds made of glass tubing, with dimensions of 4 mm diameter by 8 mm length and 4 mm diameter by 2 mm length for compressive (CS) and diametral tensile strength (DTS) tests, respectively.   The specimens for the flexural strength (FS) test were prepared using a rectangular

10   Teflon mold with dimensions of 3 mm width by 3 mm depth by 25 mm length.   The specimens were removed from molds after 15- 20 minutes, and conditioned in distilled water at 37±2°C for 1 day or 1 week, prior to testing.

EXAMPLE 18b

15   Specimen Preparation Using Visible Light Initiators

The formulations for light-curable materials were made by mixing the vinyl containing terpolymers with 0.5% (wt/wt) of d,l-camphoroquinone (CQ), 1% (wt/wt) of diphenyliodonium chloride (DC), 2-hydroxyethyl methacrylate (HEMA) or vinyl-

20   containing amino acid (i.e., AGA or ABA) and distilled water. Glass powder used in this study was the powder used in the Vitremer tri-cure glass-ionomer system (3M Dental Products), with a powder/liquid ratio (P/L) of 2.5/1 as recommended by 3M Dental Products.   Four to five specimens for each formulation

25   were prepared for flexural strength (FS) tests.   Specimens were fabricated similar to the procedures as described in Example 17, except that the curing process was completed by using an EXAKT 520 Blue Light Polymerization Unit (9W/71, GmbH, Germany) and a split Teflon mold with a glass window for

30   light exposure was used. The specimens were removed from molds after 15-20 minutes, and conditioned in distilled water at 37±2°C for 1 day or 1 week, prior to testing.

28

EXAMPLE 18c

Strength Measurements

Testing of specimens was performed on a screw-driven mechanical testing machine (Model Sintech/2G, MTS Systems Corp., Eden Prairie, MN, USA), with a crosshead speed of 1 mm/min for both diametral tensile strength (DTS) and flexure strength (FS) measurements. The FS test was performed in three-point bending, with a span of 20 mm between supports. The sample sizes were n = 5 to 9 for all three tests.

The diametral tensile strength was determined from the relationship $DTS = 2P/\pi dt$, where P = the load at fracture, d = the diameter of the cylinder and t = the thickness of the cylinder. The flexure strength in three-point bending was obtained using the expression $FS = 3Pl/2bd^2$, where P = the load at fracture, l = the distance between the two supports, b = the breadth of the specimen, and d = the depth of the specimen.

To establish controls, the Fuji II glass ionomer (GC America), Vitremer light-cured glass-ionomer (3M Dental product), and Fuji II light-cured control (GC America) (commercially available) were prepared per manufacturing directions for comparison and model systems. Their mechanical strengths are shown in all the related tables and figures.

EXAMPLE 18d

Bond Strength Measurement

Freshly extracted human molars were embedded in acrylic resin with the buccal surface facing up. The specimens were ground using a series SiC papers (240, 400, and 600 grit) to expose a superficial dentin surface. A Teflon mold having a cylindrical hole 2mm in diameter and 5 mm in depth was secured over the dentin surface to establish a bonding area. Two groups of bonded specimens were prepared for each formulation. In the first group, the 600 grit surface was bonded directly.

29

In the second group, the dentin surface was treated with 37% phosphoric acid gel for 15 seconds and then washed and dried of excess water using an air syringe. All surfaces were kept moist until bonded. A thin layer of adhesive liquid with no

5   glass was placed on the dentin surface and cured for 10 seconds. The cement mix was then placed in the cavity to achieve a thickness of 2mm and photocured for 40 seconds using a Demetron (Demetron Corp.) light-curing unit. The mold was removed and the samples were stored 24 hours at 37°C before

10 shear testing.

    The shear test was conducted by securing the samples in a SynTech tensile tester (MTS Systems, Minneapolis, MN) with the bonded specimen perpendicular to the crosshead containing a knife-edge shearing blade. The surface of the tooth was

15 brought flush to the shear blade and secured so that the blade hit at the junction of the bonded specimen and the tooth substrate. The test was run at 0.5mm/minute. The shear strength was calculated by dividing the maximum breaking force by the area of the bonded specimen.

20 EXAMPLE 19

Inventive Glass-Ionomer Bone Cement Based on Photo Initiation Systems

    The specimens made in Example 18b were evaluated using the methods described in Example 18c and results are shown in

25 Table 4, and in Figures 2 and 3. In Table 4, XM1, XM14, XM15 and XM16 were the cements with the same copolymer (i.e., AA-IA-MGA) but with different liquid formulations and different comonomers, whereas Vitremer was the commercially available light-cured glass-ionomer cement. The Vitremer glass was used

30 to formulate the inventive glass-ionomer cements. The cements were conditioned in distilled water at 37°C for 1 week.

Table 4. Mechanical Strengths of Visible Light Initiated Hybrid Amino Acid Modified Glass-Ionomer Cements*

Material	Liquid Formulation (wt)	FS [MPa] (S.D.)	CS [MPa] (S.D.)	DTS [MPa] (S.D.)	BM [GPa] (S.D.)	Toughness (N·mm)	Comonomer
XM1	55:15:30	92.1 (10.4)	201.9 (9.16)	34.91 (4.48)	1.19 (0.02)	15.9 (2.04)	HEMA
XM14	45:20:35	86.6 (2.77)	238.9 (21.4)	39.40 (6.01)	1.45 (0.03)	13.4 (0.59)	ABA
XM15	40:30:30	76.3 (8.20)	265.1 (20.5)	36.38 (3.48)	1.27 (0.32)	12.4 (1.23)	AGA
XM16	55:15:30	82.8 (4.86)	259.0 (12.4)	41.10 (5.19)	1.57 (0.06)	13.1 (0.61)	AGA
Vitremer	–	87.9 (1.35)	172.7 (8.40)	31.30 (2.94)	1.19 (0.04)	15.0 (0.16)	–

5   *Liquid formulation was composed of IEM grafted terpolymer/comonomer/water; Grafting ratio = 25% (mole %); BM = bending modulus; Toughness = area under the load-displacement curve.

10   Results in Table 4 showed that all the glass-ionomer cements of the present invention were comparable to commercial light-curable product, Vitremer, in most mechanical properties, but significantly higher in CS, DTS, and BM.

EXAMPLE 20

15   Inventive Glass-Ionomer Cement Based on Photo Initiation Systems

The specimens made in Example 18b were evaluated using the methods described in Example 18c. The results are shown in Figures 6, 7, 8 and 9. The copolymer used was the same as in Example 19. The commercially available GC Fuji II LC glass was used to formulate the inventive glass-ionomer cements. The cements were conditioned in distilled water at 37°C for 1 week. Figure 6 shows the compressive strength of the cements and viscosities of the polymer liquids composed of six amino acid derivatives, HEMA and AA. The liquid formulation was 50/25/25 based on polymer/comonomer/water and the P/L ratio was 2.7/1. Among them, AA had the highest compressive strength followed by AASPA, MBA, MGA, ABA, GA, ASPA and HEMA. The

viscosity (x 10^{-3} cp) of the liquid was in the decreasing order: MASPA > AASPA > MGA > AGA > ABA > MBA > HEMA > AA. Considering strength and working property of the cement, the MBA-containing cement had the lowest viscosity and highest

5   compressive strength. Figure 7 shows the effect of liquid formulation on CS and viscosity.   Both compressive strength and viscosity increased with increasing polymer content. The greater the polymer content in the formulation, the higher were the mechanical strengths. As shown in Figure 8, the compressive

10   strength of the cement increased with an increase of P/L ratio. However, when the ratio reached 2.7/1, the CS did not increase but instead reached a plateau. Figure 9 shows the difference between the MBA-modified cement and GC Fuji II LC cement. The MBA modified cement exhibited significantly higher CS

15   (259 MPa), DTS (26.7 MPa) and FS (71.7 MPa), compared to corresponding 216, 16 and 37 MPa for GC Fuji II LC cement.
     EXAMPLE 21
     Shear Bond Strength of Inventive Glass-Ionomer Cement Grafted with Pendent IEM

20   The specimens made in Example 18b were evaluated using the methods described in Example 18d.   The results are shown in Table 5.   In Table 5, A2, B2 and C2 were the cements containing the same terpolymers but with different amounts of polyacrylic acid.   The copolymer was used as the same as in

25   Example 19. The commercially available GC Fuji II LC glass was used to formulate the inventive glass-ionomer cements. Polyacrylic acid was also used in some of the formulations. Surface treatment of the dentin was divided into etching and non-etching as described in Example 18d. The cements were

30   conditioned in distilled water at 37°C for 1 week.

Table 5.   Shear Bond Strength (SBS) of Hybrid Amino Acid
Modified Glass-Ionomer Cements Grafted with IEM, formulating
with an Amino Acid Comonomer and polyacrylic acid

Material	SBS [MPa] Ethed(S.D.)	SBS [MPa] Non-etched(S.D.)	Polyacrylic acid added (wt %)
A2	11.4(0.41)	19.5 (4.8)	0
B2	11.1(5.42)	15.1 (4.1)	6
C2	7.41(2.68)	19.9 (4.2)	13
Fuji II LC	12.0(4.07)	N/A	N/A

5   *Grafting ratio = 25%; P/L ratio = 2/1; Liquid formulation =
50:20:30; ABA was used as comonomer; Cements were light-cured
and were conditioned in distilled for 7 days before testing.

EXAMPLE 22
10   Inventive Glass-Ionomer Bone Cement Based on Redox Initiation

Systems

     The polymers synthesized in Example 12 and specimens made

in Examples 18a and b were evaluated using the methods

described in Example 18c and results are shown in Tables 6, 7

15 and 8, and Figure 4.   In Table 6, A1, B1 and C1 were the

cements with different liquid formulations; In Table 7, D1 to

G1 were the cements with different grafting ratios.   In Table

8, L1 to O1 were the cements with different P/L ratios.   Fuji

II was the commercially available glass-ionomer cement.   The

20 Fuji II LC glass was used to formulate the inventive glass-

ionomer cements.   The cements were conditioned in distilled

water at 37°C for 1 week.

Table 6. Mechanical Strengths of Redox Initiated Hybrid Amino
Acid Modified Glass-Ionomer Cements - Effect of Components in
25 Liquid Formulation on Properties*

Material	Liquid Formulation (wt)	CS [Mpa] (S.D)	DTS [Mpa] (S.D)	CT (min)
A1	40/30/30	182.7 (7.72)	26.5 (2.98)	1.92
B1	50/18/32	192.2 (8.07)	28.6 (3.11)	2.08
C1	60/15/25	185.0 (23.8)	27.5 (4.18)	3.22
Fuji II	-	185.8 (47.9)	18.0 (0.30)	-

*Grafting ratio = 15%; P/L ratio = 2/1; Amount of activator (ascorbic acid)= 0.3%; ABA was used as comonomer; CT = curing time.

Table 7.   Effect of IEM Grafting Ratio on Polymer on Properties*

Material	Grafting Ratio (molar ratio)	Liquid Formulation (wt)	CS [Mpa] (S.D)	DTS [Mpa] (S.D)	CT (min)
D1	15%	40/30/30	182.7 (7.72)	26.5 (2.98)	1.92
E1	30%	40/30/30	173.8 (3.24)	29.6 (4.46)	2.13
F1	15%	60/15/25	185.0 (23.8)	27.5 (4.18)	3.22
G1	30%	60/15/25	227.1 (10.4)	25.4 (4.98)	3.42

*P/L ratio = 2/1; Amount of activator = 0.3%.

Material	P/L Ratio (wt)	CS (MPa) (S.D)	DTS (MPa) (S.D)	CT (min)
L1	1.5/1	162.9 (10.3)	26.9 (2.77)	2.32
M1	2.0/1	192.2 (8.07)	28.6 (3.11)	2.70
N1	2.5/1	212.5 (8.41)	30.5 (5.25)	2.05
O1	3.0/1	232.7 (13.7)	31.0 (5.67)	1.75

*Grafting ratio = 15%; Amount of activator = 0.3%; Ratio for liquid formulation = 50/18/32.

Mechanical strengths of redox-initiated glass-ionomer cements of the present invention and the effects of grafting ratios and P/L ratios are described in Tables 6, 7 and 8. The redox system exhibited improved DTS and comparable CS, compared to the Fuji II control, as shown in Table 6. Different grafting seems not to have much effect on mechanical strengths of the cements.   The higher the P/L ration, the higher the CS and DTS, as shown in Table 8.

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EXAMPLE 23

Inventive Glass-Ionomer Bone Cement Grafted with pendent GM

The polymers synthesized in Example 13 and specimens made following Example 18 were evaluated using the methods described in Example 18c and results are shown in Table 9 and Figure 5. In Table 9, A, B, D, E and H were the cements with different liquid formulations initiated with visible light, whereas F was the cement initiated using redox system. The Fuji II LC glass was used to formulate the inventive glass-ionomer cements. The cements were conditioned in distilled water at 37°C for 1 week.

Table 9. Mechanical Strengths of Hybrid Amino Acid Modified Glass-Ionomer Cements Grafted with Glycidyl Methacrylate* and containing an Amino Acid Comonomer

Material	Liquid Formulation (wt)	P/L Ratio	Grafting Ratio	FS [MPa] (S.D.)	CS [MPa] (S.D.)	DTS [MPa] (S.D.)	Initiation
A	50:20:30	2.7	15%	68.1 (8.5)	199.3 (7.9)	34.1 (1.8)	LC
B	60:15:25	2.7	15%	83.2 (3.8)	199.6 (3.7)	30.4 (1.8)	LC
D	50:20:30	2.0	15%	69.2 (2.4)	174.8 (12.6)	32.9 (2.3)	LC
E	50:20:30	3.5	15%	65.7 (3.5)	208.5 (6.3)	37.1 (2.2)	LC
F	50:20:30	2.7	15%	64.0 (4.5)	221.3 (12.5)	35.1 (4.3)	Redox
H	50:20:30	2.7	30%	80.0 (11.9)	207.8 (10.3)	37.3 (2.2)	LC
Fuji II	–		–	18.0 (0.3)	189.5 (19.4)	21.6 (3.2)	–

*In liquid formulation, poly(acrylic acid-co-itaconic acid) copolymer was used instead of poly(acrylic acid-co-itaconic acid-co-methacryloyl glutamic acid) terpolymer; Glycidyl methacrylate was used as a grafting agent; The specimens were conditioned for 1 week prior to testing; LC stands for photo-initiation, whereas redox represents redox initiation.

As shown in Table 9, all glycidyl methacrylate grafted polycarboxylic acid-containing glass ionomers exhibited much higher values in FS (64.0 to 83.2 Mpa), CS (174.8 to 221.3

Mpa) and DTS (30.4 to 37.3 Mpa) compared to Fuji II control
(18.0 in FS, 189.5 in CS and 21.6 in DTS), even though there
was no amino acid incorporated into the polymer backbone.

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       All patent and non-patent publications cited in this
specification are indicative of the level of skill of those
skilled in the art to which this invention pertains.   All
these   publications   and   patent   applications   are   herein
10 incorporated by reference to the same extent as if each
individual publication or patent application was specifically
and individually indicated as being incorporated by reference
herein.

       Although the invention herein has been described with
15 reference to particular embodiments, it is to be understood
that   these   embodiments   are   merely   illustrative   of   the
principles and applications of the present invention.   It is
therefore to be understood that numerous modifications may be
made   to   the   illustrative   embodiments   and   that   other
20 arrangements may be devised without departing from the spirit
and scope of the present invention as defined by the appended
claims.